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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/580,588

05/25/2006

Yutaka Sashida

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EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

03/25/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/580,588	Applicant(s) SASHIDA ET AL.	
	Examiner NIZAL S. CHANDRAKUMAR	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-70 is/are pending in the application.
- 4a) Of the above claim(s) 39-54 and 56-69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-38, 55 and 70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>01/17/2008</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, including claims 36-38, 55 and 70 covering compounds in the reply filed on 02/14/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 36-70 are pending.

Claims 39-54, withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/14/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

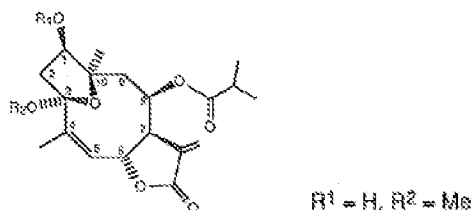
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Pereira et al. (Phytochemistry (1997), 45(7), 1445-1448, which teach on page 1446).

Pereira et al. teach,

Art Unit: 1625



corresponding to the instantly claimed compound of formula II.

Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Gonzalez (Journal of Natural Products (1994), 57(3), 400-2), provided by the applicant) which teaches on page 40, column on the right, structure 2, same as the compound of claim 38. The instant claim recites that the 3-hydroxy-1-butenyl is in a 3S-configuration which is opposite of Gonzalez depiction of stereochemistry at C9 (as R). Gonzalez's stereochemical assignment was an "assumption" based on biogenetic grounds (see page 401, column 1, last paragraph) coupled with extension of NMR data obtained for blumenol A. Gonzalez's assignment was re-investigated by Calis et al. Phytochemistry (2002), 59, 451-457, resulting in unequivocal assignment for C9 of blumenol as S (see page 453, column 1, line 9).

Comparison of NMR data for compound TD-5, i.e., the compound of claim 38, and that of Gonzalez's compound, shows (see page 21 of the specification), that the instantly reported numbers are shifted by approximately 0.07 ppm, presumably due to NMR measurements at different field strength.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

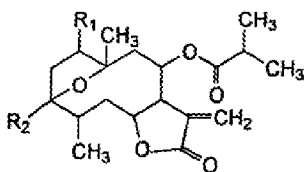
Art Unit: 1625

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

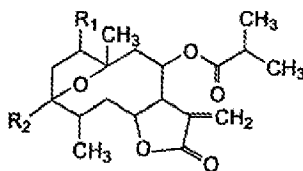
Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baruah et al. (Journal of Organic Chemistry, 1979, (44)11, 1831) in view of Zdero et al. Phytochemistry (1987), 26(7), 1999-2006.

Claim 36 is drawn to compound



wherein R1 is hydroxy and R2 represents methoxy.

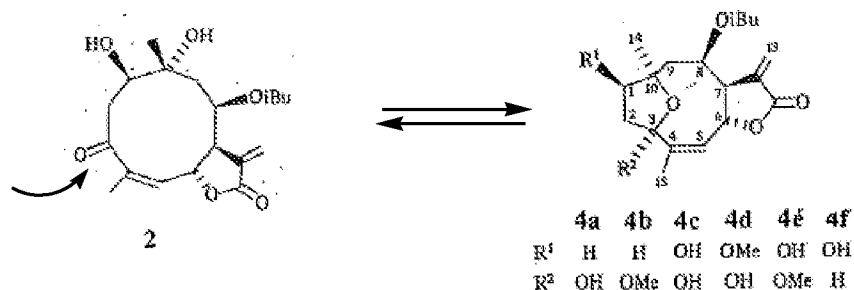
Baruah et al. teach



wherein R1 is hydroxy and R2 represents hydroxy.

The difference is the R2 group in the prior art is methyl homolog of the compound of the instant claim.

Zdero et al. teach, the equilibrium shown below.



The equilibrium is between the closed and open position, keto group shown by the arrow and the hydroxyl at C-9, forming hemiketal (and hemiketal-methyl ether) (based on whether water or methanol is present). Further, Zdero et al. state that page 2000, right-hand column, line 8-9, that the O-methyl ether(s) may be artifacts as methanol was used for extraction (similar to the extraction procedures of the instant application) and that all these compounds are obviously biogenetically related product (see line 1 of the same paragraph).

The difference between the instantly claimed hemiketal-methyl ether and compounds 4 of Zdero is the double bond between 4-5 positions shown for Zdero's compounds; in the instant case, there is single bond between 4-5 positions. It would be obvious to one of ordinary skill in the art of organic chemistry, that the 4-5 double bond is non-participant in the equilibrium shown above as well as a non-participant in the methyl ether formation. Parallel equilibrium and methyl ether formation is suggested for the compound of Baruah et al. and the compound of the instant claim.

Claims 55 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over prior art references shown below:

Claims 55 and 70 are drawn to compounds of claim 36 and 60 respectively, obtained by the process of chromatographic purification/isolation. All these compounds are biogenetically related and are routinely isolated by chromatographic purification. Numerous references cited by the applicant on pages 6 and 7 shown below as well as references cited by the Examiner

Art Unit: 1625

Patent document 1: Japanese Patent No. 2609780

Patent document 2: Japanese Patent Application No. 127538/1996

Technical Document 1: Raghwendra Pal, et al. Indian Journal of Chemistry, Section B: Organic Chemical Including Medicinal Chemistry, 14B, 259 - 262 (1976).

Technical Document 2: Raghwendra Pal, et al. Indian Journal of Chemistry, Section B: Organic Chemical Including Medicinal Chemistry, 15B, 208 - 211 (1977).

Technical Document 3: Schuster A, et al. Phytochemistry, 31, 3139 - 3141 (1992).

Technical Document 4: Paulo Sergio Pereira, et al. Phytochemistry, 45, 1445 - 1448 (1997).

Technical Document 5: C. Zdero et al. Phytochemistry, 26, 1999 - 2006 (1987).

Technical Document 6: Raghwendra Pal, et al. Indian Journal of Chemistry, Section B: Organic Chemical Including Medicinal Chemistry, 15B, 208 - 211 (1977).

Technical Document 7: Baruah Nabin C, et al. Journal of Organic Chemistry, 44, 1831 - 1835 (1979).

Technical Document 8: Antonia G. Gonzalez, et al, Journal of Natural Products, 57, 400 - 402 (1994)

Technical Document 9: Raghwendra Pal, et al. Journal of Pharmaceutical Science, 65, 918 - 920 (1976).

Technical Document 10: Raghwendra Pal, et al. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry, 15B, 208-211 (1977)

Technical Document 11: Isao Agata, et al. Yakugaku zasshi, 101, 1067-1071 (1981)

Technical Document 12: S. Shibata, et al. Yakugaku Zasshi, 80, 620-624 (1960)

Technical Document 13: Christa Zdero, et al. Phytochemistry, 26, 1999-2006 (1987)

are drawn to chromatographic separation of these biogenetically and structurally related compounds.

Nothing unobvious is seen in the methods of instant process and the processes of the above-cited references.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-38 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to diastereomerically different compounds represented by structural formulae I and II. Thus for example, formula I, 128 unique compounds are possible. It is unclear what compound the applicant is seeking protection for.

However, in claim 38, applicant specifically refers to stereochemically defined structure to negate possible rejections of this claim under 35 USC § 102(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for two compounds, does not reasonably provide enablement for over 200 compounds claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are drawn to many structurally, complex but biogenetically, related compounds (see above rejection under 35 U.S.C. 112, (second paragraph). Since no synthetic methods or methods of inter-converting and or isomerizing existing stereocenters is not presented in the specification, it is clear that presently claimed compounds are from natural sources. Because of the (enzymatic) nature of

Art Unit: 1625

biosynthesis is inherently stereospecific, and provide only one stereoisomers. (There are very few, if any, exception but found in this class of compounds.) Because of this elegance of Nature, the number of conceivable compounds in the instant case is limited to one for each formula. As such the disclosure in the specification is not commensurate with the breadth of the claims.

Claims 36-38, 55 and 70 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625

Application/Control Number: 10/580,588
Art Unit: 1625

Page 9